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10/547,206	05/19/2006	Alain Jacquet	VB60107	4723

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SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
ROONEY, NORA MAUREEN	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/08/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/547,206	JACQUET, ALAIN	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,29 and 30* is/are pending in the application.

4a) Of the above claim(s) *1-14,20-23,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-19 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-27 and 29-30 are pending.

2. Applicant's election without traverse of Group VI, claims 15-19 and 24-28, in the reply filed on 07/31/2008 is acknowledged.

3. Claims 1-14, 20-23 and 29-30 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/31/2008.

4. Claims 15-19 and 24-27 are currently under examination as they read on *Dermatophagoides pteronyssinus* ProDer p 3 or PreProDer p 3 protein allergen or derivative thereof, wherein said ProDer p 3, PreProDer p 3 or allergen derivative has a significantly reduced allergenic activity compared to Der p3; and immunogenic composition comprising said protein, and a recombinant allergen having the sequence of SEQ ID NO: 19.

5. Applicant's IDS document filed on 08/26/2005 is acknowledged.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 15-19 and 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 and 24 recite allergenic proteins 'ProDer p 3' and 'PreProDer p 3.' These terms

are indefinite because they only describe the proteins of interest by arbitrary names, 'ProDer p 3' and 'PreProDer p 3.' While the names may have some notion of the specificity of the proteins, there is no recitation which distinctly claims the proteins. For example, others in the field may isolate the same proteins and give them entirely different names. Applicants should particularly point out and distinctly claim the 'ProDer p 3' and 'PreProDer p 3 allergenic proteins by claiming a sufficient number of characteristics associated with the proteins. Claiming biochemical molecules by a particular name given to them by various workers in the field fails to distinctly claim the protein.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 15-19 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: the Pre-Pro-Der p 3 allergen of SEQ ID 19, the Pro-Der-p 3 allergen of amino acids 19-262 of SEQ ID NO:19, the mature Der p 3 allergen of amino acids 30-262 of SEQ ID NO:19 and compositions thereof; does not reasonably provide enablement for: a *Dermatophagoides pteronyssinus* ProDer p 3 **or** PreProDer p 3 protein allergen **or derivative thereof**, wherein said ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof** has a reduced allergenic activity compared to Der p3 of claim 15; wherein said allergen **or derivative** has been **thermally treated** of claim 16; wherein said allergen **or derivative** has been **genetically mutated** of claim 17; wherein **the mutation comprises a mutation of a cysteine residue** of claim 18; a recombinant allergen having the sequence of: SEQ ID NO: 19 of

claim 19; an **immunogenic composition** comprising a Dermatophagoides pteronyssinus ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof** as claimed in claim 15, or a polynucleotide encoding a *Dermatophagoides pteronyssinus* ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof**, and, optionally, an adjuvant of claim 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses the cloning and sequencing of Pre-Pro-Der p 3 of SEQ ID NO:19 having an 18 amino acid signal peptide and an 11 amino acid N-terminal Pro-sequence. The specification also discloses the use of recombinant Pro-Der p 3 in an ELISA to detect the degree of IgE binding as compared to IgE binding to Der p 3 isolated from mites (In particular, Example 11 and Figure 11).

The specification does not adequately disclose the use of any derivative or mutant of Pre-Pro-Der p 3 or Pro-Der p 3 for use in the claimed invention. The terms derivative and mutant encompass any Pre-Pro-Der p 3 or Pro-Der p 3 allergen having any number of additions, deletions or substitutions, including any two or more amino acid fragment of Pre-Pro-Der p 3 or Pro-Der p 3, though such a small fragment would not bind IgE or stimulate T cells. The specification has not adequately disclosed the genus of such derivatives and mutants for use in the claimed invention for diagnosis or therapy. Other than the Pre-Pro-Der p 3 allergen of SEQ ID 19, the Pro-Der-p 3 allergen of amino acids 19-262 of SEQ ID NO:19 and the mature Der p 3 allergen of amino acids 30-262 of SEQ ID NO:19 there is insufficient guidance as to which amino acid residues can be changed and to which amino acid residues to result in a modified protein with decreased allergenic activity. Given the lack of sufficient guidance and predictability in determining which modifications would lead to a decrease in IgE binding, it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of the claimed invention. Blumenthal et al. teaches that correlations between structure and IgE binding (or the lack of IgE binding) cannot be predicted on an a priori structural basis (PTO-892, Reference W, see entire document and page 39 of third full paragraph). Further, the art of Kinnunen et al. (PTO-892, Reference U, abstract, discussion) teaches that allergen peptide "derivatives" or altered peptide ligands (APL) of the lipocalin allergen induce differential T cell stimulation (In particular, Table I, page 6, paragraph spanning left and right columns). The discussion cautions those who are looking to use APL in allergen immunotherapy because some T cell populations, such as pathogenic memory cells, are induced by particular APLs and

exacerbate allergic disease (allergenic activity) (In particular, page 7, left column, second paragraph). One of ordinary skill in the art would be required to determine how alterations to each position of the derivates and mutants affect binding to IgE and T cell activation. The unpredictibility in the art highlights that an undue amount of experimentation is necessary to practice the claimed invention.

The specification has not adequately disclosed allergens that have been "thermally treated" for use in the claimed invention. The term "thermally treated" is not sufficiently limiting because all allergens are "thermally treated" at whatever temperature they are maintained at in storage or experiments. The specification provides no limiting definition for thermal treatment, so all Pre-Pro-Der p 3 or Pro-Der p 3 allergens are encompassed by the instant claim recitation. The specification teaches the heat denaturation of Der p 1, but not Der p 3. It is not known whether heat denaturation is effective to decrease allergenic activity. The art shows that whether an allergen that is denatured becomes less allergenic is unpredictable. For example, in Maleki et al. it is demonstrated that denaturation of peanut proteins by roasting increases binding to serum IgE from allergic individuals at approximately 90 fold higher levels than undenatured peanuts. (PTO-892, Reference V, page 767 first paragraph of discussion). Given the lack of guidance and examples in the specification, determining whether heat will denature allergens and make them less allergenic is highly unpredictable. Therefore, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention as recited.

Also at issue is whether compositions comprising the genus of allergens and derivatives encompassed by the instant claim recitations will be "immunogenic" with "reduced allergenic

activity compared to Der p 3." For reasons stated *supra*, it is unpredictable whether the genus of derivatives and mutants will generate increased allergenic activity or no immune response at all. Because of this, one of ordinary skill in the art would be required to perform undue experimentation to practice the invention commensurate in scope with the claims.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claims 15-19 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: the Pre-Pro-Der p 3 allergen of SEQ ID 19, the Pro-Der-p 3 allergen of amino acids 19-262 of SEQ ID NO:19, the mature Der p 3 allergen of amino acids 30-262 of SEQ ID NO:19 and compositions thereof.

Applicant is not in possession of: a *Dermatophagoides pteronyssinus* ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof**, wherein said ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof** has a reduced allergenic activity compared to Der p3 of

claim 15; wherein said allergen **or derivative** has been **thermally treated** of claim 16; wherein said allergen **or derivative** has been **genetically mutated** of claim 17; wherein **the mutation comprises a mutation of a cysteine residue** of claim 18; a recombinant allergen having the sequence of: SEQ ID NO: 19 of claim 19; an **immunogenic composition** comprising a Dermatophagoides pteronvssinus ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof** as claimed in claim 15, or a polynucleotide encoding a *Dermatophagoides pteronyssinus* ProDer p 3 or PreProDer p 3 protein allergen **or derivative thereof**, and, optionally, an adjuvant of claim 24.

Applicant has disclosed only the Pre-Pro-Der p 3 allergen of SEQ ID 19, the Pro-Der-p 3 allergen of amino acids 19-262 of SEQ ID NO:19, the mature Der p 3 allergen of amino acids 30-262 of SEQ ID NO:19 and compositions thereof; therefore, the skilled artisan cannot envision all the contemplated allergen and immunogenic composition possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known

or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 15-19 and 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 1995/15976 (PTO-892; Reference N).

WO 1995/15976 teaches the pre-pro-Der p III allergen of reference SEQ ID NO:2 that is 100% identical over length and sequence to instant SEQ ID NO:19 with reduced allergenic activity (In particular, reference SEQ ID NO:2, pages 35-36, page 10, lines 12-13), genetically modified pre-pro-Der p III allergens comprising a cysteine residue mutation (In particular, page 10, lines 20-3, page 14, lines 16 to page 15, line 10), immunogenic compositions thereof comprising adjuvants such as polyoxyethylene oleyl ether and n-hexadecyl polyethylene ether (a polyethylene ether) (In particular, page 20, lines 12-14 and 17-18), and wherein the allergen is administered in oil and water emulsions (dispersions) (In particular, page 20, line 24 to page 21, line 35).

Claim 16 is included in this rejection because the recitation of "thermally treated" is inherent. The specification provides no limiting definition of "thermally treated," so the broadest reasonable definition of the term encompasses maintenance of the allergen at any temperature, including room temperature.

The reference teachings anticipate the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 19, 2008

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Maher M. Haddad/
Maher M. Haddad, Ph.D.
Primary Examiner,
Art Unit 1644